CLAIMS

1. A method for treating and/or preventing and/or ameliorating obesity or other diseases and conditions characterized by excess body fat deposits, the method comprising down-regulating ghrelin by immunizing against autologous ghrelin in an animal, including a human being, the method comprising effecting presentation to the animal's immune system of an immunogenically effective amount of an immunogen selected from the group consisting of

- at least one ghrelin polypeptide or subsequence thereof which has been formulated so that immunization of the animal with the ghrelin polypeptide or subsequence thereof induces production of antibodies against the animal's autologous ghrelin, and

- at least one ghrelin analogue that incorporates into the same molecule at least one B-cell epitope of ghrelin and at least one chemical moiety not derived from ghrelin so that immunization of the animal with the analogue induces production of antibodies against ghrelin.

2. A method for increasing body mass in an animal, such as a human being, the method comprising up-regulating autologous ghrelin in the animal by immunizing against autologous ghrelin in an animal, including a human being, the method comprising effecting presentation to the animal's immune system of an immunogenically effective amount of an immunogen selected from the group consisting of

- at least one ghrelin polypeptide or subsequence thereof which has been formulated so that immunization of the animal with the ghrelin polypeptide or subsequence thereof induces production of antibodies against the animal's autologous ghrelin, and

- at least one ghrelin analogue that incorporates into the same molecule at least one B-cell epitope of ghrelin and at least one chemical moiety not derived from ghrelin so that immunization of the animal with the analogue induces production of antibodies against ghrelin.

3. The method according to claim 1 or 2, wherein the immunogen is a ghrelin analogue.

4. The method according to claim 3, wherein the analogue has preserved a substantial fraction of ghrelin B-cell epitopes and wherein the analogue also comprises

- at least one foreign T helper lymphocyte epitope (T_H epitope), and/or

- at least one first moiety which effects targeting of the analogue to an antigen presenting cell (APC) or a B-lymphocyte, and/or

- at least one second moiety which stimulates the immune system, and/or

- at least one third moiety which optimises presentation of the analogue to the immune system.

5. The method according to claim 4, wherein the foreign T_H epitope and/or the first and/or the second and/or the third moiety is/are present in the analogue by being bound to suitable side groups ghrelin or a subsequence thereof.

6. The method according to claim 4 or 5, wherein the analogue is a ghrelin polypeptide that is modified by at least one amino acid substitution and/or deletion and/or insertion and/or addition.

7. The method according to claim 6, wherein the analogue is a fusion polypeptide.

8. The method according to claim 6 or 7, wherein the amino acid substitution and/or deletion and/or insertion and/or addition allows for a substantial preservation of the overall tertiary structure of ghrelin in the analogue.

9. The method according to any one of claims 4 and 5-8, insofar as these depend on claim 4, wherein the analogue includes duplication of at least one ghrelin B-cell epitope and/or introduction of a hapten.

10. The method according to any one of claims 4 and 5-9, insofar as these depend on claim 4, wherein the foreign T-cell epitope is immunodominant in the animal.

11. The method according to any one of claims 4 and 5-10, insofar as these depend on claim 4, wherein the foreign T-cell epitope is promiscuous.

12. The method according to claim 11, wherein the at least one foreign T-cell epitope is selected from a natural promiscuous T-cell epitope and an artificial MHC-II binding peptide sequence.

13. The method according to claim 12, wherein the natural T-cell epitope is selected from a Tetanus toxoid epitope such as P2 or P30, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, and a *P. falciparum* CS epitope.

14. The method according to any one of claims 4 and 5-13, insofar as these depend on claim 4, wherein the first moiety is a substantially specific binding partner for a B-lymphocyte specific surface antigen or for an APC specific surface antigen, such as a hapten or a carbohydrate for which there is a receptor on the B-lymphocyte or the APC.

15. The method according to any one of claims 4 and 5-14, insofar as these depend on claim 4, wherein the second moiety is selected from a cytokine and a heat-shock protein.

16. The method according to claim 15, wherein the cytokine is selected from, or is an effective part of, interferon γ (IFN-γ), Flt3L, interleukin 1 (IL-1), interleukin 2 (IL-2), interleukin 4 (IL-4), interleukin 6 (IL-6), interleukin 12 (IL-12), interleukin 13 (IL-13), interleukin 15 (IL-15), and granulocyte-macrophage colony stimulating factor (GM-CSF), and the heat-shock protein is selected from, or is an effective part of any of, HSP70, HSP90, HSC70, GRP94, and calreticulin (CRT).

17. The method according to any one of claims 4 and 5-16, insofar as these depend on claim 4, wherein the third moiety is of lipid nature, such as a palmitoyl group, a myristyl group, a farnesyl group, a geranyl-geranyl group, a GPI-anchor, and an N-acyl diglyceride group.

18. The method according to any of the preceding claims wherein the immunogen comprises a substitution of at least one amino acid sequence within the ghrelin polypeptide with an amino acid sequence of equal or different length which gives rise to a foreign T_H epitope in the analogue.

19. The method according to any of the preceding claims, wherein the ghrelin polypeptide comprises an amino acid sequence corresponding to amino acids 24-51 in SEQ ID NO: 11 or a subsequence thereof, wherein is inserted an amino acid sequence that gives rise to a foreign T_H epitope in the analogue or wherein at least one amino acid sequence is substituted by an amino acid sequence of equal or different length so as to give rise to a foreign T_H epitope in the analogue, wherein the introduction is performed after any one of amino acids 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, and 117 in SEQ ID NO: 11, and wherein amino acid 1 and/or 2 and/or 3 and/or 4 and/or 5 and/or 6 and/or 7 and/or 8 and/or 9 and/or 10 and/or 11 and/or 12 and/or 13 and/or 14 and/or 15 and/or 16 and/or 17 and/or 18 and/or 19 and/or 20 and/or 21 and/or 22 and/or 23 and/or 24 and/or 25 and/or 26 and/or 27 and/or 28 and/or 29 and/or 30 and/or 31 and/or 32 and/or 33 and/or 34 and/or 35 and/or 36 and/or 37 and/or 38 and/or 39 and/or 40 and/or 41 and/or 42 and/or 43 and/or 44 and/or 45 and/or 46 and/or 47 and/or 48 and/or 49 and/or 50 and/or 51 and/or 52 and/or 53 and/or 54 and/or 55 and/or 56 and/or 57 and/or 58 and/or 59 and/or 60 and/or 61 and/or 62 and/or 63 and/or 64 and/or 65 and/or 66 and/or 67 and/or 68 and/or 69 and/or 70 and/or 71 and/or 72 and/or 73 and/or 74 and/or 75 and/or 76 and/or 77 and/or 78 and/or 79 and/or 80 and/or 81 and/or 82 and/or 83 and/or 84 and/or 85 and/or 86 and/or 87

and/or 88 and/or 89 and/or 90 and/or 91 and/or 92 and/or 93 and/or 94 and/or 95 and/or 96 and/or 97 and/or 98 and/or 99 and/or 100 and/or 101 and/or 102 and/or 103 and/or 104 and/or 105 and/or 106 and/or 107 and/or 108 and/or 109 and/or 110 and/or 111 and/or 112 and/or 113 and/or 114 and/or 115 and/or 116 and/or 117 in SEQ ID NO: 11 may be deleted.

20. The method according to claim 19, wherein the analogue is selected from the group consisting of polypeptides having an amino acid sequence selected from SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5.

21. The method according to claim 20, wherein the immunogen has polyamino acids covalently or non-covalently linked to a carrier molecule capable of effecting presentation of multiple copies of antigenic determinants, wherein the polyamino acids are selected from the group consisting of a ghrelin polypeptide, a ghrelin subsequence, and a ghrelin analogue.

22. The method according to claim 21, wherein the carrier molecule contains or consists of a pharmaceutically acceptable activated polyhydroxypolymer.

23. The method according to claim 22 insofar as it depends on claim 4, wherein the polyhydroxypolymer serves as a carrier backbone to which are separately bound 1) a ghrelin polypeptide or subsequence thereof and 2) a foreign T_H epitope.

24. The method according to claim 22 or 23, wherein the polyamino acids are bound to the polyhydroxypolymer via a bond cleavable by a peptidase, such as an amide bond or a peptide bond.

25. The method according to claim 24, wherein the polyamino acids provide for the nitrogen moiety of their respective amide bond.

26. The method according to any one of claims 22-25, wherein the polyhydroxypolymer carrier is substantially free of amino acid residues.

27. The method according to any one of claims 22-26, wherein the polyamino acids are bound to the activated polyhydroxypolymer via the nitrogen at the N-terminus of the amino acid sequence.

28. The method according to any of one of claims 22-27 wherein the polyhydroxypolymer is water soluble.

29. The method according to any one of claims 22-26 wherein the polyhydroxypolymer is water insoluble.

30. The method according to any one of claims 22-29, wherein the polyhydroxypolymer is selected from naturally occurring polyhydroxy compounds and synthetic polyhydroxy compounds.

31. The method according to any one of claims 22-30, wherein the polyhydroxypolymer is a polysaccharide.

32. The method according to claim 31, wherein the polysaccharide is selected from the group consisting of acetan, amylopectin, gum agar-agar, agarose, alginates, gum Arabic, carregeenan, cellulose, cyclodextrins, dextran, furcellaran, galactomannan, gelatin, ghatti, glucan, glycogen, guar, karaya, konjac/A, locust bean gum, mannan, pectin, psyllium, pullulan, starch, tamarine, tragacanth, xanthan, xylan, and xyloglucan.

33. The method according to claim 32, wherein the polyhydroxypolymer is dextran.

34. The method according to any one of claims 22-30, wherein the polyhydroxypolymer is selected from the group consisting of highly branched poly(ethyleneimine)(PEI), tetrathienylene vinylene, Kevlar (long chains of poly-paraphenyl terephtalamide), Poly(urethanes), Poly(siloxanes), polydimethylsiloxane, silicone, Poly(methyl methacrylate) (PMMA), Poly(vinyl alcohol), Poly(vinyl pyrrolidone), Poly(2-hydroxy ethyl methacrylate), Poly(N-vinyl pyrrolidone), Poly(vinyl alcohol), Poly(acrylic acid), Polytetrafluoroethylene (PTFE), Polyacrylamide, Poly(ethylene-co-vinyl acetate), Poly(ethylene glycol) and derivatives, Poly(methacrylic acid), Polylactides (PLA), Polyglycolides (PGA), Poly(lactide-co-glycolides) (PLGA), Polyanhydrides, and Polyorthoesters.

35. The method according to any of claims 22-34, wherein the average molecular weight of the polyhydroxypolymer before activation is at least 500.

36. The method according to any one of claims 22-35, wherein the polyhydroxypolymer is activated with functional groups selected from tresyl (trifluoroethylsulphonyl), maleimido, p-nitrophenyl cloroformate, and tosyl (p-toluenesulfonyl).

37. The method according to any of claims 22-36 that further comprises at least one further polyamino acid is coupled to the polyhydroxypolymer, said at least one further polyamino acid being selected from the group consisting of an immune stimulating peptide or a targeting peptide.

38. The method according to any one of the preceding claims, wherein an effective amount of the immunogen is administered to the animal via a route selected from the parenteral route such as the intradermal, the subdermal, the intracutaneous, the subcutaneous, and the in-

tramuscular routes; the peritoneal route; the oral route; the buccal route; the sublinqual route; the epidural route; the spinal route; the anal route; and the intracranial route.

39. The method according to claim 38, wherein the effective amount is between 0.5 µg and 2,000 µg of the ghrelin polypeptide, the subsequence thereof or the analogue thereof.

40. The method according to claim 37 or 38, wherein the ghrelin polypeptide or analogue is contained in a virtual lymph node (VLN) device.

41. The method according to any one of claims 38-40, wherein the ghrelin polypeptide, the subsequence thereof, or the ghrelin analogue has been formulated with an adjuvant which facilitates breaking of autotolerance to autoantigens.

42. The method according to any one of claims 1-20, wherein presentation of the immunogen to the immune system is effected by introducing nucleic acid(s) encoding the immunogen into the animal's cells and thereby obtaining *in vivo* expression by the cells of the nucleic acid(s) introduced.

43. The method according to claim 42, wherein the nucleic acid(s) introduced is/are selected from naked DNA, DNA formulated with charged or uncharged lipids, DNA formulated in liposomes, DNA included in a viral vector, DNA formulated with a transfection-facilitating protein or polypeptide, DNA formulated with a targeting protein or polypeptide, DNA formulated with Calcium precipitating agents, DNA coupled to an inert carrier molecule, DNA encapsulated in chitin or chitosan, and DNA formulated with an adjuvant.

44. The method according to claim 43, wherein the nucleic acid(s) is/are contained in a VLN device.

45. The method according to any one of claims 38-44, which includes at least one administration/introduction per year, such as at least 2, at least 3, at least 4, at least 6, and at least 12 administrations/introductions.

46. An analogue of a ghrelin polypeptide which is derived from an animal ghrelin polypeptide wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the animal's autologous ghrelin polypeptide and which is as defined in any one of claims 4-37.

47. An immunogenic composition comprising an immunogenically effective amount of an analogue according to claim 46, the composition further comprising a pharmaceutically and immunologically acceptable carrier and/or vehicle and optionally an adjuvant.

48. A nucleic acid fragment which encodes an analogue as defined in any one of claims 4-20.

49. A vector carrying the nucleic acid fragment according to claim 48, such as a vector that is capable of autonomous replication.

50. The vector according to claim 49, which is selected from the group consisting of a plasmid, a phage, a cosmid, a mini-chromosome, and a virus.

51. The vector according to claim 49 or 50, comprising, in the 5'→3' direction and in operable linkage, a promoter for driving expression of the nucleic acid fragment according to claim 48, optionally a nucleic acid sequence encoding a leader peptide enabling secretion of or integration into the membrane of the polypeptide fragment, the nucleic acid fragment according to claim 48, and optionally a terminator.

52. The vector according to any one of claims 49-51 which, when introduced into a host cell, is capable or incapable of being integrated in the host cell genome.

53. The vector according to claim 51 or 52, wherein a promoter drives expression in a eukaryotic cell and/or in a prokaryotic cell.

54. A transformed cell carrying the vector of any one of claims 49-53, such as a transformed cell which is capable of replicating the nucleic acid fragment according to claim 48.

55. The transformed cell according to claim 54, which is a microorganism selected from a bacterium, a yeast, a protozoan, or a cell derived from a multicellular organism selected from a fungus, an insect cell such as an S_2 or an SF cell, a plant cell, and a mammalian cell.

56. The transformed cell according to claim 54 or 55, which expresses the nucleic acid fragment according to claim 48, such as a transformed cell, which secretes or carries on its surface, the analogue according to claim 46.

57. The method according to any one of claims 1-20, wherein presentation to the immune system is effected by administering a non-pathogenic microorganism or virus which is carrying a nucleic acid fragment which encodes and expresses the ghrelin polypeptide, subsequence or analogue.

58. A composition for inducing production of antibodies against a ghrelin polypeptide in the autologous host, the composition comprising

- a nucleic acid fragment according to claim 48 or a vector according to any one of claims 49-53, and

- a pharmaceutically and immunologically acceptable carrier and/or vehicle and/or adjuvant.

59. A stable cell line which carries the vector according to any one of claims 49-53 and which expresses the nucleic acid fragment according to claim 48, and which optionally secretes or carries the analogue according to claim 46 on its surface.

60. A method for the preparation of the cell according to any one of claims 54-56, the method comprising transforming a host cell with the nucleic acid fragment according to claim 48 or with the vector according to any one of claims 49-53.